

II. The Claims Are Not Obvious Under 35 U.S.C. § 103

A. Greenberger in view of Coyle and Applicants' disclosure

The Office has rejected claims 47, 61-65, 67, 69-75, 78-79, and 81 under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,599,712 to Greenberger ("Greenberger") in view of Coyle *et al.*, Science, 262:689-695 (1993) ("Coyle"), and Applicants' disclosure. (Office Action, pages 2-4.) Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness, there must be some teaching, suggestion, or motivation in the prior art to lead one of ordinary skill in the art to modify or combine the teachings of the references in the manner proposed by the Office. *Pro-Mold and Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Cir. 1996); M.P.E.P. § 2143. The combination of references must also provide a reasonable expectation of success. *In re Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). The suggestion or motivation must be found in the prior art, not in Applicant's disclosure (*id.*) and it must be clear and particular. *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999). Thus, while a person of ordinary skill in the art may possess the requisite knowledge and ability to modify the prior art, that modification is not obvious unless the prior art suggested the desirability of such a modification. *In re Gordon*, 733 F.2d 900, 902 (Fed. Cir. 1984).

Applicants contend that the Office has failed to establish a *prima facie* case of obviousness. There simply is no clear and particular suggestion in the prior art to combine *Greenberger's* teachings of protecting cells from the damaging effects of anti-cancer drugs and ionizing radiation using adenoviral vectors encoding an SOD

gene with the disease states described in the secondary references, as proposed by the Office.

Greenberger is directed to "protecting an individual's tissues and cells against the damaging effects of an agent that elicits the production of a free radical, superoxide anion, or heavy metal cation when that individual is exposed to an agent." *Greenberger*, col. 1, lines 7-11. Specifically, *Greenberger* concerns protecting a cancer patient's tissues and cells from the damaging effects of anti-cancer drugs and ionizing radiation. *Id.*, title, abstract, and col. 1, line 1, to col. 3, line 15. The Office alleges that *Greenberger* "teaches that it is a object of the invention to '...provide a safe and efficient method of transferring oxidation or cation-scavenging protein encoding genes directly into a patient's cells.'" Office Action, page 3. The Office admits that *Greenberger* "does not teach the use of the recited adenoviral vectors to treat the specific diseases recited by the applicants." *Id.* The Office alleges that the secondary references, Coyle and Applicants' specification, cure the deficiencies of *Greenberger* because they disclose that free radicals are recognized as being involved in certain diseases. *Id.* The Office concludes that it would have been obvious to combine *Greenberger*, Coyle and Applicants' disclosure "because *Greenberger et al.* teaches that said vectors can be used to safely and efficiently deliver SOD genes to patients so as to scavenge excess free radicals which Coyle et al. and applicants disclose are well known to be associated with diseases such as ALS, diabetes, etc." *Id.*, page 4.

Applicants point out that the only "patients" that *Greenberger* teaches or suggests are cancer patients being treated with an agent that elicits the production of free radicals. *Greenberger* is specifically concerned with preventing the toxic effects

of the exogenous agents, *i.e.*, chemotherapy and/or ionizing radiation, administered to the patients. As pointed out, the Office admits that Greenberger “does not teach the use of the recited adenoviral vectors to treat the specific diseases recited by the applicants.” Office action, page 3. Moreover, Applicants submit that nothing in Greenberger teaches or suggests using Greenberger’s adenoviral vector for treating or preventing any disease. Greenberger merely discloses methods for preventing the toxic side-effects of anti-cancer therapies.

Coyle is primarily concerned with reviewing the role of oxidative stress in neuronal diseases, with particular emphasis on the contribution of glutamate (Glu) receptor activation. Coyle, however, states that “[i]t would be incorrect to conclude that oxidative stress is the sole mechanism responsible for Glu-induced neuronal degeneration in vivo, because the delayed effects of acute monovalent ionic shifts...and Ca^{2+} activation of proteases, kinases, and nucleases likely contribute.” Coyle, page 694, col. 1. Coyle also points out that “[u]nrelated primary pathogenic processes may compromise neuronal function...such as amyloid A4 peptide in Alzheimer’s disease. *Id.*, cols. 1 and 2. Therefore, Coyle teaches that mechanisms and pathways not directly related to oxidative stress are also important for the course and pathology of neurodegenerative disorders of the brain. Accordingly, Coyle’s teaching would not have motivated one of ordinary skill in the art to use the adenoviral vectors of Greenberger to treat the diseases disclosed in Coyle or Applicants’ specification.

Furthermore, the Office points to Applicants disclosure at page 2 that it is “nowadays recognized that these free radicals are involved in [certain disorders or diseases]” as evidence of motivation to combine the cited references to devise the

claimed invention. This disclosure, however, merely recognizes that free radicals are involved in these disorders or diseases. Applicants submit that one of ordinary skill in the art would also know that that other mechanisms and pathways not directly related to free radicals are also important for the course and pathology of these disorders and diseases. Accordingly, the cited disclosure in Applicants' specification does not provide clear and particular evidence that one of ordinary skill in the art reading the cited references would be motivated to combine the cited references to use the adenoviral vectors of Greenberger to treat the diseases disclosed in Coyle or Applicants' specification.

In view of the above, Applicants contend that the Office has merely identified a combination that might be feasible, but has not proffered clear and particular evidence concerning the desirability of making the combination. Although Greenberger's adenoviral vector may be useful for preventing the toxic effects of exogenous agents that generate free radicals, there is no clear and particular evidence that Greenberger's vector would be similarly useful for treating Coyle's diseases where excess free radicals may be involved in the disease mechanisms. Moreover, "a general incentive does not make obvious a particular result, nor does the existence of techniques by which those efforts can be carried out." *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995). At best, it may have been obvious to try such a combination, however, this is not the standard. *In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988); M.P.E.P. § 2145(X)(B).

In view of these remarks, Applicants respectfully request that the Office withdraw this rejection.

**B. Greenberger in View of Coyle,
Applicants' Disclosures, and Gregory**

The Office has rejected claims 66 and 82 under 35 USC§ 103(a) as being obvious over Greenberger in view of Coyle, Applicants' disclosure, and U.S. Patent No. 5,882,877 to Gregory *et al.* ("Gregory"). Office Action, pages 4-5. Applicants respectfully traverse the rejection.

Applicants' above remarks regarding the lack of motivation to combine Greenberger, Coyle, and Applicants' specification are herein incorporated by reference, and applied to the present rejection.

Applicants submit that Gregory does not cure the deficiencies of the combination of Greenberger, Coyle, and Applicants' specification. Accordingly, Applicants respectfully request that the Office withdraw this rejection.

**C. Greenberger in View of Coyle, Applicants'
Disclosure, Le Gal La Salle, and Nabel**

The Office has rejected claim 68 under 35 USC§ 103(a) as being obvious over Greenberger in view of Coyle, Applicants' disclosure, Le Gal La Salle *et al.*, *Science* 259:988-990 (1993) ("Le Gal La Salle"), and U.S. Patent No. 5,650,306 to Nabel *et al.* ("Nabel"). Office Action, pages 5-7. Applicants respectfully traverse the rejection.

Applicants' above remarks regarding the lack of motivation to combine Greenberger, Coyle, and Applicants' specification are herein incorporated by reference, and applied to the present rejection.

Applicants submit that Le Gal La Salle and Nabel, either together or separately, do not cure the deficiencies of the combination of Greenberger, Coyle, and Applicants' specification. Accordingly, Applicants respectfully request that the Office withdraw this rejection.

III. **CONCLUSION**

In view of the foregoing, Applicants respectfully request that the Office reconsider and withdraw the rejections of pending claims 47, 61-75, 78-79, and 81-82 as obvious over the cited art, and allow all pending claims.

Please grant any extensions of time required to enter this amendment and response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

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By: 

Charles D. Niebylski
Reg. No. 46,116

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com